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Characteristic Trends in Prevalence and Use of New Synthetic "Designer" Drugs over the Territory of the Republic of Bashkortostan

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ABSTRACT

The urgency of this study has become vivid in the light of the growing problem of prevalence and use of new synthetic drug types, incidence rate of comorbid states, and pathomorphism of psychoactive substances consumption. The aim of this paper consists in analysis and disclosure of the research data obtained on consumption of such designer drugs as amphetamines, synthetic cathinones and cannabimimetics over the whole territory of the Republic of Bashkortostan, namely, revelation of geographical regoins with increased level of drug abuse, determination of the addicts' age and gender composition. The principal method of the research involves a statistical analysis of the data obtained for the individuals examined in conjunction with the results obtained in the course of chemico-toxicological analysis of biomaterials taken from them. During this study, the regions with especial prevalence of the synthetic narcotic substances abuse were revealed, the main types of drugs especially preferred in consumption to the others were determined, and the prevailing age and gender composition of drug addicts' contingent was shown. This paper would be useful for psychiatrists, experts in narcology, as well as for personnel of institutions and agencies engaged in anti-drug activity.

KEYWORDS Synthetic drugs, cathinones, amphetamines, cannabimimetics, gas chromatography-mass spectrometry (GC-MS), spices ARTICLE HISTORY Received 20 April 2016 Revised 28 April 2016 Accepted 9 May 2016

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Introduction

Urgency of the Problem

Disorders in mental health of individuals using the so-called "designer" drugs or "spices" that have gained their popularity in Russia and some European countries starting from about 2009 attract a growing attention of specialists and researchers in the fields of psychiatry, narcology, pharmacology, and biology (Shileyko, Ayzberg and Kuzmenko, 2015). Branded as "spices" or "bath salts", these drugs are distributed mainly via the internet space by means of social networks with the help of virtual payment systems. According to the report of Russian Federal Service for Drug Control (FDCS) Director and State Anti-Drug Committee (SADC) Chairman V. P. Ivanov at the SADC meeting held on the 6th of October, 2014, on "Measures for elimination of emergency situation arising from mass poisoning by new psychoactive substances", the Republic of Bashkortostan is among the top three Russian regions most affected by "spice" addiction (Pozdnyakova, 2013)

In addition, the report established the fact that the amount of such synthetic drugs confiscations over the last seven years in Russia has grown by a factor of 130 or more, namely, from 165 kg to 22 tons (Mazhiev et al., 2015).

Sometimes, the effect of new synthetic narcotic drugs differs from that of their natural analogue so significantly that they can be spoken about as a new class of narcotic drugs appeared (Shileyko, Ayzberg and Kuzmenko, 2015). Conventionally, these drugs can be categorized into three large types:

- 1. Designer amphetamines
- 2. Synthetic cathinones
- 3. Synthetic cannabimimetics (or synthetic cannabinoids)

Amphetamines join the group of phenylethylamines which in their turn constitute the largest group of designer drugs. Phenylethylamines join the group of substances named phenylalkylamines. Besides phenylethylamines, the phenylalkylamines group includes phenylisopropylamines. Phenylalkylamines themselves form a part of still more general group of substances named arylalkylamines. This group, besides phenylalkylamines, indolealkylamines subdivided into N-substituted tryptamines, alkyltryptamines, ergolines or lysergamides, and β -carbolines (Golovko et al., 2015). The term of "designer amphetamines" covers a wide variety of drugs including methylated derivatives of amphetamine, i.e. methamphetamine (pervitin, methodrine, "ice", "speed"), 2,5-dimethoxy-4-methylamphetamine (STP), 3,4-methylenedioxyamphetamine (tenamfetamine, MDA, love drug), 3,4methylenedioxymethamphetamine (MDMA, "ecstasy"), 2,5-dimethoxy-4-bromamphetamine (DOB), 4-methoxymethamphetamine (4-MMA, para-methoxy-Nmethylamphetamine, PMMA, methylMMA) (Shileyko, Ayzberg and Kuzmenko, 2015).

Another group of "designer drugs" includes artificially produced cathinones. Natural cathinones (e.g. norephedrine) are alkaloids originally isolated from khat (*Catha edulis*), a shrub plant of *Celastraceae* family, originating from Eastern Africa. By their toxic effects, cathinones are similar to amphetamines, and sometimes are distributed under the guise of the latter. Synthetic cathinones can be divided into the following groups: phenylethylamine

derivatives, such as methylenedioxypyrovalerone (MDPV), α -PVP, α -PVT, MHPH, etc., and cathinone- β -ketones (methylone, ethylone, mephedrone etc.) (Pozdnyakova, 2013). The clinical pattern of narcotic intoxication caused by the intake of amphetamines and cathinones is characterized by an excessive physical activity, enhancement in working capacity, getting into a cheerful mood, appetite depression The side effects include anxiety, fatigue, aggressiveness, insomnia, involuntary body movements (muscular twitching, smacking of lips, etc.), as well as various somatic vegetative manifestations, such as hyperhidrosis, cardiac abnormalities, development of acute renal insufficiency, hemorrhagic and ischemic strokes. Quite often, the intake of amphetamines is accompanied by development of acute psychotic disorders or toxic psychoses in the form of visual or auditory hallucinations, delirious experiences, mental confusions, disorientation, etc (Veselovskaya, 2008). Further escalation of drug intake doses can lead to a lethal outcome (Golovko et al., 2015).

The third group of artificially produced narcotic drugs comprises synthetic cannabimimetics (SC). HU-210 compounds developed in the Jerusalem University (HU – Hebrew University) in 1988 under the supervision of Professor R. Mechoulam are considered to be parental predecessors of this group (Huffman et al., 2005). A tremendous contribution to the development of new synthetic cannabinoids was made by the research teams of Professor J. W. Huffman and Professor A. Makriyannis. According to a commonly accepted identification system, the substances developed by them were identified with JWH and AM abbreviations, respectively. For example, JWH-018; JWH-081; JWH-250; AM-2202; and AM-2201 are components most frequently detected in the samples of "spices" (Järbe et al., 2010) (Streich et al., 2014).

By now, a lot of artificial exogenous cannabinoids have been synthesized. All of them are represented by the following basic groups depending on the chemical nature of a basic parental compound. These are naphthoylindoles (JWH-007, JWH-015, JWH-018, and others); naphthylmethylindoles (JWH-175, JWH-184, JWH-185, and others); naphthoylpyrroles (JWH-030, JWH-147, JWH-307); phenylacetylindoles (JWH-167, JWH-203, JWH-250, and others); benzoylindoles (AM-630, AM-679, AM-694, and others); naphthylmethylindenes (JWH-176, and others); cyclohexylphenoles (CP-47,497 and its C8-homologue cannabicyclohexanol, CP-55,490, HU-308); adamantoylindoles (AB-001, AM-1248); cyclopropanoylindoles (UR-144, 5F-UR-144, and others) (Huffman et al., 2005).

In the period of 2012 – 2013, a number of new synthetic cannabimimetics and their analogs appeared in the market of smoking blends in some RF regions, including the Republic of Bashkortostan. By their chemical structure, these synthetic cannabimimetics can be categorized into two groups:

The first group includes synthetic cannabimimetics which are the esters of 8-hydroxyquinoline and alkylindole derivatives, i.e. PB-22, PB-22F, BB-22, FUB-PB-22 cannabimimetics. The second group includes synthetic cannabimimetics comprising derivatives of valine and alkylindazole amides. They are represented by four names: AB-PINACA, 5F-AB-PINACA, AB-FUBINACA, and AB-CHMINACA (Dvorskaya et al., 2014) (Savchuk et al., 2015). Recently, the territory of the Republic of Bashkortostan has seen a significant spread of indole-3-carboxylates and indazole-3-carboxamides. In the illegal market of

narcotic and psychotropic substances, these drug species are represented by quinolin-8-yl-1-pentylfluoro-1H-indole-3-carboxylate (PB-22F) (Figure 1a) and N-[1-carbamoyl-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (AB-Chminaca) (Figure 1b).

Figure 1. Structural formulas of synthetic cannabimimetics: a) PB-22F of alkylindole group; b) AB-CHMINACA of alkylindazole group.

Permanent drug consumers experience progressive drug addiction and withdrawal (abstinence) syndrome. The drug addiction syndrome is usually manifested by an increase in tolerance (frequently up to 5-7 times), including pharmacological tolerance, inability to stop drug intake, disregard of day duties and interests, development of abstinence syndrome. The abstinence syndrome is manifested by psychic disorders, such as asthenia, insomnia, evident anxiety up to the onset of paranoiac reactions(Järbe et al., 2010), hysterical and depressive presentations, retention of pronounced addiction to the drug, neurological symptoms, i.e. tremor, obvious inconsistencies when performing coordination tests, hyperreflexia, apparent vegetative manifestations, nystagmus, somatic symptoms, dramatic decrease in bodyweight, profuse sweat, hyperthermic manifestations, tachycardia, headaches, nausea (Golovko et al., 2015) (Kaklyugin, 2014) (Zobnin, Stadler, 2014).

The principal condition for preventing the abuse of narcotic drugs of this type is permanent monitoring and revealing new species of cannabimimetics, as well as determining their metabolites in biological materials.

The purpose of this study consisted in the analysis of synthetic drugs consumption pattern over the territory of the Republic of Bashkortostan (hereafter referred to as RB). The following tasks were set:

- to reveal the age, gender and geographical patterns of the synthetic narcotic drug consumption over the RB territory;
- to determine the groups with highest risk of drug dependence development over the RB territory;

In the course of the research, chemico-toxicological and statistical methods were used.

Methodological Framework

Base of Research

Biological material taken from 3458 individuals aged from 16 to 84 years and resided on the territory of RB was used. As biomaterial for examination, urine of tested individuals was taken, since urine is the most convenient biological object for drug detection due to a low content of protein components.

All tested individuals had been registered for regular medical check-up in Republican Narcological Dispensary No.1 of the Ministry of Health of RB or had passed a thorough medical examination for the presence of narcotic drugs in their organisms in 2015. All the urine samples of examined individuals were found to be positive for pharmaceuticals and/or narcotic or psychotropic substances. The examination was conducted by a written voluntary consent of tested individuals or their legal representatives (in case of minors). This work was carried out in chemico-toxicological laboratory, as well as in the 1st hospital of BPHF Republican Narcological Dispensary No.1 of RB Ministry of Health.

Research Methods

Chemico-toxicological methods. A chemico-toxicological analysis consists in detection of psychotropic substances and/or products of their metabolism in biological liquids of human organism (Kurdil, 2015) (Nikolaeva et al., 2015) (Savchuk, Gofenberg, 2013). At present, the main method used for the qualitative determination of metabolites of most synthetic cannabimimetics and so-called "bath salts" is gas chromatography - mass-spectrometry (GC-MS). In our investigation, we used an Agilent 7820 gas chromatograph with an Agilent 5975 mass selective detector (Agilent, USA), a HP-5MS capillary column with 25 mm inner diameter, 30 m length, and film thickness of 0.25 µm. Sample preparation was performed by means of non-enzymatic hydrolysis. Sample derivatization to improve detection of synthetic cannabimimetics was performed by modifying their metabolites through methylation and acetylation. The obtained chromatograms were analyzed for identification of sample components using ChemStation G1701DA and AMDIS (The Automatic Mass Spectral Deconvolution and Identification System, NIST) software products.

Statistical methods. The examined individuals were stratified by the place of residence, gender, and according to Erikson's psychosocial age-related periodization (with amendments). All the examined persons were divided into four age groups, namely, "Childhood" of 1-19 years old persons (hereafter Group I), "Youth" of 20-35 years old persons (hereafter Group II), "Maturity" of 36-60 years old persons (hereafter Group III), and "Senility" of 61 years old and older persons (hereafter Group IV) (Erikson, 1996). Distribution of frequencies was analyzed in groups of individuals resided on the RB territory and discriminated by their gender, age and residence. Statistical calculations were performed using Microsoft Excel 2010 software.

Results and Discussion

General Characteristics of Narcotization by Synthetic Preparations Over the Territory of the Republic of Bashkortostan

From the whole sample (86% male, 14% female), the individuals whose biological liquids in this examination were positive for synthetic drugs, i.e. amphetamines and their derivatives, such as methamphetamines, artificial cannabimimetics and cathinones were selected for the research.

The level of narcotization by synthetic drugs in the total number of examined individuals amounted to 53%. It was found that the most consumable synthetic drug over the RB territory was alpha-pyrrolidinovalerophenone (thereafter α -PVP), which is a synthetic cathinone or "bath salt". The second most spread group of drugs was that of synthetic cannabimimetics, or more exactly, the alkylindazole derivative AB-CHMINACA. More detailed information is presented in Table 1.

Table 1. Structure of synthetic drug use in the Republic of Bashkortostan.

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Type of synthetic drug	% of a total number of consumers		
Amphetamines and their derivatives	1.3 %		
(methamphetamines)			
synthetic cathinones	75.2 %		
(alpha-PVP and MDPV)			
Indole synthetic cannabimimetics	1.8 %		
(PB-22F, XLR-11)			
Indazole synthetic cannabimimetics	21.7 %		
(AB-PINACA, 5F-AB-PINACA, AB-PINACA-F, AB-			
CHMINACA, AB-FUBINACA, ADB-CHMINACA, MDMB-			
BZ-F, MDMB-CHMINACA)			

The share of multiple synthetic drug users (poly-addicts) in the total number of people consuming designer drugs within the examined sample of individuals amounted to 3.6 %. They also preferred α -PVP and AB-CHMINACA. Three quarters of poly-addicts used these two drugs in combination.

Identification of RB Regions with Elevated Levels of Synthetic Drugs Consumption

For determination of narcotization levels in different parts of RB, we took into account an official administrative and territorial division of RB. The mean level of consumption was found to be 34.15 individuals (per administrative-territorial entity). Those RB districts where consumption levels exceeded the above figure were regarded to as problematic. There were revealed 8 problematic districts out of the total of 54. These were the districts of Belebey, Beloretsk, Krasnokamsk, Kuyurgaza, Meleuz, Sterlitamak, Tuimazy, and Ufa. More detailed information is presented in Table 2.

Table 2. Districts of the Republic of Bashkortostan with elevated levels of synthetic drugs consumption.

total District of ... of the Levels exceeding the average number of addicts level over all RB districts (factors) Belebey 3 % 1.61 3.4 % Beloretsk 1.67 Krasnokamsk 6.9 % 3.79 2.2 % Kuyurgaza 1.23 Meleuz 5.5 % 2.96 Sterlitamak 9.1 % 4.92 1.41 **Tuimazy** 2.6 % 50.2 % Ufa 27.70

It was found that the greatest number of synthetic drug consumers falls on RB districts of Ufa and Sterlitamak. This fact can be explained by the fact that Ufa and Sterlitamak are the largest RB cities. Most of the other RB districts with elevated levels of designer drugs consumption were contiguous with neighboring regions of Russian Federation, such as the Republic of Tatarstan and Chelyabinsk Region. This can indicate the possible routes of the synthetic drugs supply to RB.

We estimated the structure of the synthetic drugs consumption in the problematic RB districts. In total, the average figures in them do not significantly differ from those obtained for the Republic of Bashkortostan as a whole. More detailed information is presented in Table 3.

Table 3. Structure of synthetic drugs consumption in problematic districts of the Republic of Bashkortostan.

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District of	Alpha-PVP	AB-CHMINACA	Other drugs
Belebey	0.87	0.11	0.02
Beloretsk	0.50	0.39	0.11
Krasnokamsk	0.89	0.08	0.03
Kuyurgaza	0.66	0.24	0.10
Meleuz	0.50	0.46	0.04
Sterlitamak	0.70	0.21	0.09
Tuimazy	0.88	0.06	0.06
Ufa	0.79	0.13	0.08
X ±σ	0.70±0.15	0.23±0.14	0.06±0.03

Note: Hereafter X is mean value, σ is standard deviation.

The data obtained show that the most preferable synthetic drug consumed in these districts, as well as over the Republic of Bashkortostan on the whole, is α -PVP. The second most preferable drug is designer cannabimimetic AB-CHMINACA which is frequently detected in composition of the so-called "spices". The analysis of the data presented in Table 3 also indicates the enhanced consumption of AB-CHMINACA in Districts of Beloretsk and Meleuz. This fact can be explained by relative cheapness of this drug and possibly by age peculiarities of addicts.

Determination of Age and Gender Composition of Synthetic Drug Addicts

Gender and age peculiarities of the examined addicts were estimated over the RB districts with elevated levels of synthetic drugs consumption. Detailed information is presented in Table 4.

Table 4. Gender and age peculiarities of addicts from districts of the Republic of Bashkortostan with elevated levels of synthetic drugs consumption.

District of	Gender composition		Age peculiarities		
	male	female	Group I	Group II	Group III
Belebey	0.75	0.25	0.02	0.62	0.36
Beloretsk	0.91	0.09	0.07	0.46	0.47
Krasnokamsk	0.85	0.15	0.03	0.58	0.39
Kuyurgaza	0.83	0.17	0.02	0.60	0.38
Meleuz	0.95	0.05	0.13	0.58	0.29
Sterlitamak	0.91	0.09	0.04	0.71	0.25

Tuimazy	0.85	0.15	0.02	0.58	0.40
Ufa	0.92	0.08	0.13	0.67	0.20
X ±σ	0.87±0.06	0.13±0.06	0.06 ± 0.05	0.60±0.07	0.34±0.09

Investigation of gender composition of synthetic narcotic drug consumers from problematic districts of RB showed that mean gender composition of addicts in these districts was much the same as in the Republic of Bashkortostan as a whole. The detailed analysis of sex distribution among the drug addicts demonstrated that the greatest number of female synthetic drug consumers was observed for the residents of the District of Belebey (0.25); the second greatest number of such consumers was recorded in the District of Kuyurgaza.

The analysis of age peculiarities in designer drugs consumption over the problematic RB districts showed that in two districts (Ufa and Meleuz) there is more than a twofold excess (0.13 versus 0.06) in the number of consumers relating to a "Childhood" group (1-19 years old persons), i.e. Group I in Table 4. It could be evidence of an extremely upsetting tendency towards adolescent narcotization in these districts of the Republic of Bashkortostan. In general, the age structure of synthetic drugs consumption was characterized by a predominance of young addicts (Group II in Table 4). The only exception was the District of Beloretsk where the "Maturity" group (36-60 years old persons) (Group III in Table 4) prevailed with a slight overbalance (about 0.01). This fact could possibly be attributed to adult (mature) addicts transition from consumption of narcotic drugs made of natural raw materials to consumption of synthetic drugs. Besides the District of Beloretsk, the share of mature addicts was also large in the Districts of Krasnokamsk (0.39) and Tuimazy (0.40). Measures of early diagnostics, medical examination, and social adaptation of addicts, as well as suppression of the ways of synthetic drugs supply would significantly reduce the number of designer drug addicts on the territory of the Republic of Bashkortostan.

Conclusions

- It was found that consumption of such synthetic narcotic drugs as alphapyrrolidinovalerophenone (α-PVP) and AB-CHMINACA on the territory of the Republic of Bashkortostan prevails over the other types of synthetic "designer" drugs.
- Eight districts of the Republic of Bashkortostan with elevated levels of synthetic narcotic drugs consumption were revealed. These were the Districts of Belebey, Beloretsk, Krasnokamsk, Kuyurgaza, Meleuz, Sterlitamak, Tuimazy, and Ufa.
- It was shown that the dominating group of "designer" narcotic drug addicts in the Republic of Bashkortostan is that of males aged 20-35.

Recommendations

This paper would be useful for any officials of narcological patient care institutions, narcological psychiatrists, experts in narcology and preventology, as well as for personnel of institutions and agencies engaged in anti-narcotics activity.

Disclosure statement

No potential conflict of interest was reported by the authors.

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